

AMENDMENTS TO THE CLAIMS

1. **(Currently Amended)** A method of making an antibody molecule, the antibody containing an immunoglobulin heavy chain comprising a $\alpha 3$ domain or a mu domain, the method comprising:

- (a) ~~Providing~~providing a nucleotide sequence encoding an immunoglobulin heavy chain molecule;
- (b) ~~Modifying~~modifying the nucleotide sequence to form a modified nucleotide sequence, wherein the modifying is in the region of the nucleotide sequence encoding the C-terminus 18 amino acids of the immunoglobulin heavy chain molecule to remove, or reduce the effectiveness of, one or more vacuolar targeting signal of the encoded immunoglobulin heavy chain;
- (c) ~~Inserting~~inserting the modified nucleotide sequence into a host plant cell; and
- (d) ~~Causing~~causing the host plant cell to (i) express the modified nucleotide sequence to form a modified immunoglobulin heavy chain, (ii) co-express an immunoglobulin light chain and (iii) secrete the modified immunoglobulin heavy chain and an immunoglobulin light chain from the host plant cell.

2-33. **(Cancelled)**

34. **(Previously Presented)** A method according to claim 1 wherein the immunoglobulin heavy chain molecule is IgA, IgM or an IgA/G hybrid.

35. **(Previously Presented)** A method according to claim 1 wherein the nucleotide sequence is modified by at least one of the modifications selected from the group consisting of

- (i) one or more point mutations of the nucleotide sequence,

- (ii) deleting one or more nucleotides,
- (iii) adding one or more nucleotides and
- (iv) replacing one or more nucleotides with a synthetic nucleotide sequence.

36. **(Previously presented)** A method according to claim 35, wherein the synthetic nucleotide sequence encodes an amino acid sequence of general formula:

$-(Xaa_1)_m C(Xaa_2)_n$

where: C = a cysteine residue

Xaa₁ = independently any amino acid with the proviso that it is not from I, L or forms a consecutive sequence X₁ X₂ X₃ V S X₄ (SEQ ID NO: 1)

where: X₁ = N, H or L

X₂ = V or Y

X₃ = S or N

X₄ = aliphatic amino acid

Xaa₂ = independently any amino acid

m = at least 2

n = 0 to 5.

37. **(Previously presented)** A method according to claim 36, wherein Xaa₂ is Y and n = 1.

38. **(Previously Presented)** A method according claim 1, wherein nucleotides encoding the last 16 amino acids of the immunoglobulin heavy chain are deleted.

39. **(Previously Presented)** A method according to claim 1 wherein the resultant amino acid sequence at the C terminus of the immunoglobulin heavy chain has a formula selected from the group consisting of:

- (a) SCMVGHEALPMNFTQKTIDRLSGKPACY (SEQ ID NO: 7),
- (b) SCMVGHEALPMNFTQKTIDRLSGKPAAACY (SEQ ID NO: 8),
- (c) SCMVGHEALPMNFTQKTIDRLSGKPHASTPEPDPVACY (SEQ ID NO: 9) and
- (d) SCMVGHEALPMNFTQKTIDRLSGKPAAAAACY (SEQ ID NO: 69).

40. **(Previously Presented)** A method according to claim 1 wherein the nucleotide sequence of part (a) originally encoded the amino acid sequence:

$X_1 X_2 X_3 V S X_4$ (SEQ ID NO: 1)

where: $X_1 = N, H$ or L

$X_2 = V$ or Y

$X_3 = S$ or N

$X_4 =$ aliphatic amino acid.

41. **(Previously presented)** A method according to claim 40, wherein the amino acid sequence is: $N V S V S V$ (SEQ ID NO: 2).

42. **(Previously Presented)** A method according to claim 1 wherein the nucleotide sequence of part (a) encoded L or I .

43. **(Previously Presented)** A method according to claim 42, wherein the modified nucleotide sequence encodes a modified amino acid selected from the group consisting of:

(i) an isoleucine 3 amino acids from the C-terminus end of the immunoglobulin heavy chain,

(ii) an isoleucine 10 amino acids from the C-terminus end of the immunoglobulin heavy chain and

(iii) an isoleucine 3 amino acids from the C-terminus end of the immunoglobulin heavy chain and an isoleucine 2 amino acids from the C-terminus end of the immunoglobulin heavy chain.

44. **(Previously Presented)** A method according to claim 1, wherein the modified nucleotide sequence is contained within a nucleotide sequence encoding the sequence:

$P T X_1 X_2 X_3 V S X_4 X_5 X_6 X_7 X_8 X_9 X_{10} X_{11} X_{12} C X_{13}$ (SEQ ID NO: 5)

where: $X_1 = N, H$ or L

$X_2 = V$ or Y

$X_3 = S$ or N

$X_4 =$ an aliphatic amino acid

$X_5 =$ an aliphatic amino acid

$X_6 = M, V$ or L

X_7 = S or A
 X_8 = E or D
 X_9 = any amino acid
 X_{10} = D, E, G or A
 X_{11} = G or S
 X_{12} = I, T, V, Z or A
 X_{13} = may or may not be present and, where present is A or Y.

45. **(Currently Amended)** A method of adding J-chain binding capability to the immunoglobulin heavy chain of an antibody comprising the steps of:

- (a) providing a nucleotide encoding an immunoglobulin heavy chain;
- (b) adding to that nucleotide a nucleotide sequence encoding a synthetic tail with the amino acid sequence:

$-(Xaa_1)_m C(Xaa_2)_n$

where: C = Cys

Xaa₁ is independently any amino acid with the proviso that it is not I or L or forms a consecutive sequence X₁ X₂ X₃ V S X₄ (SEQ ID NO: 1) (where X₁ = N, H or L; X₂ = V or Y; X₃ = S or N; X₄ = aliphatic amino acid)

Xaa₂ = independently any amino acid

m = at least 2

n = 0 to 5; and

- (c) expressing the immunoglobulin nucleotide in a host plant cell to form an immunoglobulin heavy chain capable of binding J-chain, and
- (d) co-expressing an immunoglobulin light chain in said host plant cell.

46. **(Cancelled)**

47. **(Cancelled)**

48. **(Currently Amended)** A method according to ~~claim 46~~ claim 1, wherein the plant cell is part of a transgenic plant.

49. **(Currently Amended)** A method according to ~~claim 47~~ claim 45, wherein the plant cell is part of a transgenic plant.

50. **(Previously presented)** A method according to claim 1 additionally comprising the step of isolating and purifying the antibody molecule.

51. **(Previously presented)** A method according to claim 45 additionally comprising the step of isolating and purifying the antibody molecule.

52. **(Previously Presented)** A method according to claim 50, wherein the antibody molecule is subjected to a protease digest to produce Fab or F(ab')₂ fragments.

53. **(Previously presented)** A method according to claim 51, wherein the antibody is subjected to a protease digest to for Fab or F(ab')₂ fragments.

54. **(Previously Presented)** An antibody containing an immunoglobulin heavy chain comprising an $\alpha 3$ domain or a mu domain, the $\alpha 3$ domain or mu domain lacking one or more targeting signals towards the C-terminal end.

55. **(Previously presented)** An antibody capable of binding J-chain comprising at its C-terminal end the sequence:

$-(Xaa_1)_m C(Xaa_2)_n$

where: C = Cys

Xaa₁ is independently any amino acid with the proviso that it is not I or L or forms a consecutive sequence X₁ X₂ X₃ V S X₄ (SEQ ID NO: 1) (where X₁ = N, or L; X₂ = V or Y; X₃ = S or N; X₄ = aliphatic amino acid)

Xaa₂ = independently any amino acid

m = at least 2

n = 0 to 5

56. **(Previously presented)** An antibody according to claim 54 which does not contain the targeting signal: $X_1 X_2 X_3 V S X_4$ (SEQ ID NO: 1)

where: $X_1 = N, H \text{ or } L$

$X_2 = V \text{ or } Y$

$X_3 = S \text{ or } N$

$X_4 = \text{aliphatic amino acid.}$

57. **(Previously presented)** An antibody according to claim 55 which does not contain the targeting signal: $X_1 X_2 X_3 V S X_4$ (SEQ ID NO: 1)

where: $X_1 = N, H \text{ or } L$

$X_2 = V \text{ or } Y$

$X_3 = S \text{ or } N$

$X_4 = \text{aliphatic amino acid.}$

58. **(Previously presented)** An antibody according to claim 56, wherein the targeting signal is $N V S V S V$ (SEQ ID NO: 2).

59. **(Previously presented)** An antibody according to claim 57, wherein the targeting signal is $N V S V S V$ (SEQ ID NO: 2).

60. **(Previously presented)** An antibody according to claim 54 which contains one or no isoleucine or leucine amino acids within the last 18 amino acids at the C-terminus of the heavy chain of the antibody.

61. **(Previously presented)** An antibody according to claim 55 which contains one or no isoleucine or leucine amino acids within the last 18 amino acids at the C-terminus of the heavy chain of the antibody.

62. **(Previously presented)** An antibody according to claim 54 comprising at the C-terminus end of the heavy chain of antibody, the sequence:

$-(Xaa_1)_m C(Xaa_2)_n$

where: C = cysteine residue

Xaa₁ = independently any amino acid with the proviso that it is not I or L
or forms a consecutive sequence X₁ X₂ X₃ V S X₄ (SEQ ID NO: 2)
where: X₁ = N, H or L
X₂ = V or Y
X₃ = S or N
X₄ = aliphatic amino acid
Xaa₂ = independently any amino acid
m = at least 2
n = 0 to 5.

63. **(Previously presented)** An antibody according to claim 55 comprising at the C-terminus end of the heavy chain of antibody, the sequence:

-(Xaa₁)_m C(Xaa₂)_n
where: C = cysteine residue
Xaa₁ = independently any amino acid with the proviso that it is not I or L
or forms a consecutive sequence X₁ X₂ X₃ V S X₄ (SEQ ID NO: 2)
where: X₁ = N, H or L
X₂ = V or Y
X₃ = S or N
X₄ = aliphatic amino acid
Xaa₂ = independently any amino acid
m = at least 2
n = 0 to 5.

64. **(Previously presented)** An antibody according to claim 54 in which at least two, preferably two to four, glycine or alanine residues are present downstream of a C-terminal targeting sequence

65. **(Previously presented)** An antibody according to claim 55 in which at least two, preferably two to four, glycine or alanine residues are present downstream of a C-terminal targeting sequence

66. **(Previously presented)** An antibody according to claim 54 in which at least the terminal amino acid residue of a C-terminal targeting sequence is replaced by at least two, preferably two to four, glycine or alanine residues.
67. **(Previously presented)** An antibody according to claim 55 in which at least the terminal amino acid residue of a C-terminal targeting sequence is replaced by at least two, preferably two to four, glycine or alanine residues.
68. **(Previously presented)** A method of treating a disease by administering an antibody according to claim 54 to a patient.
69. **(Previously presented)** A method of treating a disease by administering an antibody according to claim 55 to a patient.
70. **(Previously presented)** A method of prophylaxis, comprising administering an antibody according to claim 54 to a person or animal.
71. **(Previously presented)** A method of prophylaxis, comprising administering an antibody according to claim 55 to a person or animal.
72. **(Previously presented)** A vector comprising a nucleotide sequence encoding an antibody according to claim 54.
73. **(Previously presented)** A vector comprising a nucleotide sequence encoding an antibody according to claim 55.
74. **(Previously presented)** A host cell comprising a nucleotide sequence encoding antibody according to claim 54.
75. **(Previously presented)** A host cell comprising a nucleotide sequence encoding antibody according to claim 55.
76. **(Previously presented)** A host cell comprising a vector according to claim 72.

77. **(Previously presented)** A host cell comprising a vector according to claim 73.
78. **(Previously presented)** A transgenic plant comprising a nucleotide encoding an antibody according to claim 54.
79. **(Previously presented)** A transgenic plant comprising a nucleotide encoding an antibody according claim 55.
80. **(Previously presented)** An immunoassay comprising an antibody as defined in claim 54.
81. **(Previously presented)** An immunoassay comprising an antibody as defined in claim 55.
82. **(Previously Presented)** The method of claim 1, further comprising adding to the nucleotide sequence encoding the immunoglobulin heavy chain a nucleotide sequence encoding a synthetic tail with the amino acid sequence $-(Xaa_1)_m C(Xaa_2)_n$, wherein:
- $-C = Cys$
 - Xaa_1 is independently any amino acid with the proviso that it is not I or L or forms a consecutive sequence $X_1 X_2 X_3 V S X_4$ (where $X_1 = N, H$ or L ; $X_2 = V$ or Y ; $X_3 = S$ or N ; $X_4 =$ aliphatic amino acid)
 - $-Xaa_2 =$ independently any amino acid
 - $-m =$ at least 2
 - $-n = 0$ to 5; and
- wherein said synthetic tail adds J-chain binding capability to the heavy chain of the immunoglobulin.
83. **(Cancelled)**
84. **(Currently Amended)** A method according to ~~claim 83~~ claim 1, wherein the plant cell is part of a transgenic plant.

85. **(Previously presented)** A method according to claim 82 additionally comprising the step of isolating and purifying the antibody molecule.

86. **(Previously Presented)** A method according to claim 85, wherein the antibody molecule is subjected to a protease digest to produce Fab or F(ab')₂ fragments.

87. **(Previously Presented)** The method according to claim 44, wherein at least one of X₁-X₁₃ is a member selected from the group consisting of:

X₁ = N

X₂ = V

X₄ = V or L

X₅ = I, V or L

X₆ = M

X₉ = G, V, A or T

X₁₀ = D

X₁₁ = G

X₁₂ = I or T.

88. **(Currently Amended)** A method of making an antibody molecule, the antibody containing an immunoglobulin heavy chain comprising a α 3 domain or a mu domain, the method comprising:

(a) ~~Providing~~ providing a nucleotide sequence encoding an immunoglobulin heavy chain molecule;

(b) ~~Modifying~~ modifying the nucleotide sequence to form a modified nucleotide sequence of (a) by deleting the last 16 amino acids of the immunoglobulin heavy chain molecule .

- (c) ~~Inserting~~ inserting the modified nucleotide sequence into a host plant cell; and
- (d) ~~Causing~~ causing the host plant cell to (i) express the modified nucleotide sequence to form a modified immunoglobulin heavy chain, (ii) co-express an immunoglobulin light chain, and (iii) secrete the modified immunoglobulin heavy chain and an immunoglobulin light chain from the host plant cell.

89. **(Previously Presented)** A method according to claim 88 wherein the immunoglobulin heavy chain molecule is IgA, IgM or an IgA/G hybrid.